

DOCKET NO.: CELL-0086  
Application No.: 09/450,999  
Notice of Allowance Dated: December 11, 2003

PATENT

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PATENT & TRADEMARK

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Application of:  
**John Robert Porter, et al.**  
Application No.: **09/450,999**  
Filing Date: **November 29, 1999**  
For: **β-ALANINE DERIVATIVES**

Confirmation No.: **8439**

Group Art Unit: **1624**

Examiner: **Thomas C. McKenzie**

**EXPRESS MAIL LABEL NO: EV 160092112 US**  
**DATE OF DEPOSIT: January 9, 2004**

Mail Stop Issue Fee  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

**COMMUNICATION AFTER ALLOWANCE PURSUANT TO 37 CFR § 1.312**

In response to the Notice of Allowance dated **December 11, 2003**, reconsideration is respectfully requested in view of the amendments and/or remarks as indicated below:

- Amendments to the Specification** begin on page \_\_\_\_\_ of this paper.
- Amendments to the Claims** are reflected in the listing of the claims which begins on page \_\_\_\_\_ of this paper.
- Amendments to the Drawings** begin on page \_\_\_\_\_ of this paper and include an attached replacement sheet.
- Remarks/Arguments** begin on page 2 of this paper.

**REMARKS/ARGUMENTS**

An Information Disclosure Statement was filed for the application on January 11, 2000 and was accompanied by a 1449 Form and copies of the ninety-one references listed on the form. Applicants received a return post card from the Patent Office indicating that the Information Disclosure Statement, 1449 Form, and all ninety-one listed references had been received by the Patent Office on January 14, 2000. A copy of the return post card is enclosed. Applicants have not yet received initialed copies of the 1449 Form from the Examiner. Courtesy copies of the Information Disclosure Statement, 1449 Form, and each of the listed references are being delivered directly to the Examiner. Applicants respectfully ask the Examiner to initial and return the 1449 Form to their undersigned representative prior to the due date for payment of the issue fee (March 11, 2004), confirming consideration of the listed references.

A Supplemental Information Disclosure Statement was filed for the application on April 25, 2000 and was accompanied by a 1449 Form and copies of the thirteen references listed on the form. Applicants received a return post card from the Patent Office indicating that the Information Disclosure Statement, 1449 Form, and all thirteen listed references had been received by the Patent Office on April 27, 2000. A copy of the return post card is enclosed. Applicants received initialed copies of the 1449 Form, but reference AM was not initialed and the Examiner indicated that the reference was missing. Courtesy copies of the Information Disclosure Statement, 1449 Form, and reference AM are being delivered directly to the Examiner. Applicants respectfully ask the Examiner to initial and return the 1449

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Form to their undersigned representative prior to the due date for payment of the issue fee  
(March 11, 2004), confirming consideration of reference AM.

Respectfully submitted,

**Date:** January 9, 2004

  
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PATENT AND TRADEMARK OFFICE**

**Paper:** Information Disclosure Statement (w/first class stamp, in dupl.); USPTO Form 1449 (7 Sheets); 91 References Cited / All Copies Submitted; Postcard

**Applicant(s) :** John Robert Porter et al.

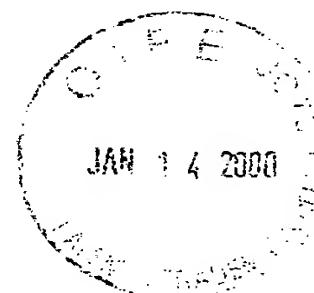
**Title:**  $\beta$ -ALANINE DERIVATIVES

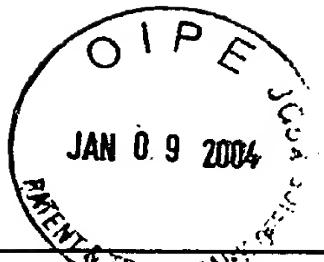
**Serial No.:** 09/450,999

**Filed:** November 29, 1999

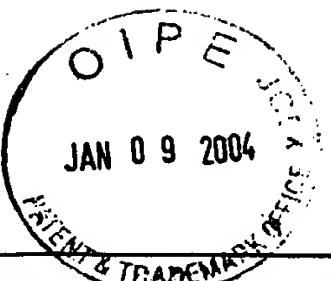
**Docket No.:** CELL-0086 (DAC/jjkeeler)

**Date Sent:** January 11, 2000





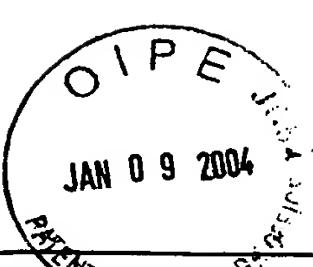
<b>Form PTO-1449 Modified</b>		
List of Patent and Publications Cited by Applicant (Use several sheets if necessary)		
U.S. Department of Commerce Patent and Trademark Office		
Docket No. <b>CELL-0086</b>		Serial No. <b>09/450,999</b>
Applicant <b>John Robert Porter, John Clifford Head, Graham John Warrelow, and Sarah Catherine Archibald</b>		
Filing Date <b>November 29, 1999</b>		Group <b>Not Yet Assigned</b>
<b>OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)</b>		
AA	Abraham, W.M. et al., " $\alpha_4$ -Integrins Mediate Antigen-Induced Late Bronchial Responses and Prolonged Airway Hyperresponsiveness in Sheep," <i>J. Clin. Invest.</i> , <b>1994</b> , 93, 776-787	
AB	Bach et al., "Anomalous optical rotation and circular dichroism of N-thioacylated. $\alpha$ -amino acids and deriva," <i>Acta Chem. Scand.</i> , <b>1966</b> , 20(10), 2781-2794	
AC	Barrett, G.C., "Circular dichroism of <i>N</i> -thiobenzoyl-1- $\alpha$ -amino acids. III. Their circular dichroism through the near-ultraviolet wavelength range," <i>J. Chem. Soc.</i> , <b>1967, Section C</b> , 1-5	
AD	Berlin, C. et al., " $\alpha 4\beta 7$ Integrin Mediates Lymphocyte Binding to the Mucosal Vascular Addressin MAdCAM-1," <i>Cell</i> , <b>1993</b> , 74, 185-195	
AE	Binns, R.M. et al., "The Role of E-Selectin in Lymphocyte and Polymorphonuclear Cell Recruitment into Cutaneous Delayed Hypersensitivity Reactions in Sensitized Pigs," <i>J. Immunol.</i> , <b>1996</b> , 157, 4094-4099	
AF	Briskin, M.J. et al., "Structural Requirements for Mucosal Vascular Addressin Binding to Its Lymphocyte Receptor $\alpha_4\beta_7$ ," <i>J. Immunol.</i> , <b>1996</b> , 156, 719-726	
AG	Cardarelli, P.M. et al., "Cyclic RGD Peptide Inhibits $\alpha 4\beta 7$ Interaction with Connecting Segment 1 and Vascular Cell Adhesion Molecule," <i>J. Biol. Chem.</i> , <b>1994</b> , 269(28), 18668-18673	
AH	<i>Chemical Abstracts</i> , "N-[4-Thiazolidinyl]carbonyl]amino acid derivatives," <b>1981</b> , 95(19), Abstract No. 169173f, 1 page	
AI	Corey, E.J. et al., "A Synthetic Method for Formyl $\rightarrow$ Ethynyl Conversion (RCHO $\rightarrow$ RC≡CH or RC≡CR')," <i>Tetrahedron Lett.</i> , <b>1972</b> , 36, 3769-3772	
<b>EXAMINER</b>		<b>DATE CONSIDERED</b>



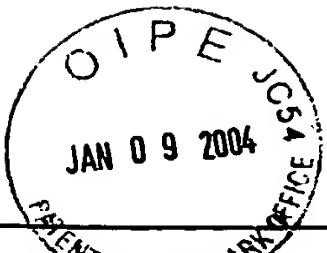
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<b>OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)</b>		
	<b>AJ</b>	Cornforth, J.W., "Oxazoles and Oxazolones," <i>Chem. Penicillin</i> , Princeton Book Review, <b>1949</b> , pages 688, 799, and 800
	<b>AK</b>	Ferguson, T.A. et al., "Two integrin-binding peptides abrogate T cell-mediated immune responses <i>in vivo</i> ," <i>Proc. Natl. Acad. Sci. USA</i> , <b>1991</b> , <i>88</i> , 8072-8076
	<b>AL</b>	Fu, H. et al., "Preliminary study on synthesis and antitumor activity in vitro of derivatives of timonacic," <i>Chemicals Abstracts</i> , <b>1988</b> , <i>108</i> (17), Abstract No. 150358k, 1 page
	<b>AM</b>	Harris, R.L.N. et al., <i>Aust. J. Chem.</i> , "Potential wool growth inhibitors. 2(1H)-Pyridone analogs of mimosine," <b>1977</b> , <i>30</i> (3), 649-655
	<b>AN</b>	Hartke, K. et al., "Dithio and thiono esters. Part 61. Synthesis of $\alpha$ -amino dithioesters and endothiodipeptides," <i>J. Prakt. Chem.</i> , <b>1996</b> , <i>338</i> (3), 251-256
	<b>AO</b>	Holzmann, B. et al., "Peyer's patch-specific lymphocyte homing receptors consist of a VLA-4-like $\alpha$ chain associated with either of two integrin $\beta$ chains, one of which is novel," <i>EMBO J.</i> , <b>1989</b> , <i>8</i> (6), 1735-1741
	<b>AP</b>	Humphries, M.J. et al., "Mechanisms of VCAM-1 and fibronectin binding to integrin $\alpha_4\beta_1$ : implications for integrin function and rational drug design," <i>Ciba Foundation Symposium</i> , <b>1995</b> , <i>189</i> , 177-194
	<b>AQ</b>	Issekutz, T.B., "Inhibition of Lymphocyte Endothelial Adhesion and In Vivo Lymphocyte Migration to Cutaneous Inflammation by TA-3, a New Monoclonal Antibody to Rat LFA-1," <i>J. Immunol.</i> , <b>1992</b> , <i>149</i> (10), 3394-3402
	<b>AR</b>	Jaynes, B.H. et al., "Synthesis and <i>In Vivo</i> Antibacterial Activity of Hygromycin a Analogs Modified at the C <sub>4</sub> ' Aryl Position," <i>Bioorg. Med. Chem. Letts.</i> , <b>1993</b> , <i>3</i> (8), 1531-1536
	<b>AS</b>	Jepson, J.B. et al., "Reactions of $\alpha$ -Thioacylamino-acids. Their conversion into Thiazolones and Derivatives Thereof," <i>J. Chem. Soc.</i> , <b>1955</b> , 1791-1797
	<b>AT</b>	Lei, H. et al., "Efficient Synthesis of a Phosphinate Bis-Amino Acid and Its Use in the Construction of Amphiphilic Peptides," <i>J. Org. Chem.</i> , <b>1994</b> , <i>59</i> , 4206-4210
	<b>AU</b>	Li, Z. et al., "Effect of an anti-Mo1 MAb on ozone-induced airway inflammation and airway hyperresponsiveness in dogs," <i>Am. J. Physiol.</i> , <b>1992</b> , <i>263</i> (6 Pt 1), L723-726
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U.S. Department of Commerce Patent and Trademark Office			Filing Date <b>November 29, 1999</b>	Group <b>Not Yet Assigned</b>
<b>OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)</b>				
	<b>AV</b>	Marlin, S.D. et al., "LFA-1 Immunodeficiency Disease," <i>J. Exp. Med.</i> , <b>1986</b> , 164, 855-867		
	<b>AW</b>	Masahiko, N., Japanese Patent No. 57-080370 published May 19, 1982, "Alpha-Methylcinnamic Acid Derivative, its Preparation and Antilipemic Agent Containing The Same," <i>Patent Abstracts of Japan</i> , <b>1982</b> , 1 page		
	<b>AX</b>	Nagasawa, H.T. et al., " $\beta$ -Substituted Cysteines as Sequestering Agents for Ethanol-Derived Acetaldehyde in Vivo," <i>J. Med. Chem.</i> , <b>1987</b> , 30, 1373-1378		
	<b>AY</b>	Noike, Y., "Synthesis of Quinolizine Derivatives. VI. Synthesis of 3-Aminoquinolizines. (1). Synthesis of <i>dl</i> -3-Amino-, <i>dl</i> -3- <i>epi</i> -Amino-, and <i>dl</i> -3- <i>epi</i> -Dimethylaminoquinolizidines," <i>Yakugaku Zasshi</i> , <b>1959</b> , 79(12), 1514-1518 (English summary included)		
	<b>AZ</b>	Ohki, S. et al., "Synthesis of quinolizine derivatives. V. Studies on Diastereoisomer of Ethyl 3-Quinolizidinecarboxylate," <i>Chem. Pharm. Bull.</i> , <b>1959</b> , 7(6), 708-712		
	<b>BA</b>	Osborne, L., "Leukocyte Adhesion to Endothelium in Inflammation," <i>Cell</i> , <b>1990</b> , 62, 3-6		
	<b>BB</b>	Osborn, L. et al., "Direct Expression Cloning of Vascular Cell Adhesion Molecule 1, a Cytokine-Induced Endothelial Protein that Binds to Lymphocytes," <i>Cell</i> , <b>1989</b> , 59, 1203-1211		
	<b>BC</b>	Podolsky, D.K. et al., "Attenuation of Colitis in the Cotton-top Tamarin by Anti- $\alpha$ 4 integrin Monoclonal Antibody," <i>J. Clin. Invest.</i> , <b>1993</b> , 92, 372-380		
	<b>BD</b>	Schultz, Von O.-E. et al., "Analogos of nuleic acid based as antimetabolites," <i>Arzneimittel Forschung. Drug Res.</i> , <b>1967</b> , 17(8), 1060-1064 (English summary included)		
	<b>BE</b>	Shroff, H.N. et al., "Small Peptide Inhibitors of $\alpha_4\beta_7$ Mediated MAdCAM-1 Adhesion to Lymphocytes," <i>Barge. Med. Chem. Letts.</i> , <b>1996</b> , 6(21), 2495-2500		
	<b>BF</b>	Sonnenberg, A., "Integrins and Their Ligands," <i>Curr. Topics Microbiol. Immunol.</i> , <b>1993</b> , 184, 7-35		
	<b>BG</b>	Springer, T.A., "Adhesion receptors of the immune system," <i>Nature</i> , <b>1990</b> , 346, 425-434		
	<b>BH</b>	Springer, T.A., "Traffic Signals for Lymphocyte Recirculation and Leukocyte Emigration: The Multistep Paradigm," <i>Cell</i> , <b>1994</b> , 76, 301-314		
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<b>OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)</b>		
	<b>BI</b>	Tsunematsu, H. et al., "Hydrolysis of phenylthiazolones of <i>p</i> -guanidinophenylalanine and arginine by trypsin and related enzymes," <i>J. Biochem.</i> , <b>1983</b> , 94(4), 1119-1125
	<b>BJ</b>	Vanderslice, P. et al., "A Cyclic Hexapeptide is a Potent Antagonist of $\alpha 4$ Integrins," <i>J. Immunol.</i> , <b>1997</b> , 158, 1710-1718
	<b>BK</b>	Yanagisawa, H. et al., WO 97/37970, "Preparation of phenylalkylcarboxylic acid derivatives lowering blood sugar level," <i>Chemical Abstracts</i> , <b>1997</b> , Abstract 127:307307, 4 pages
	<b>BL</b>	Yang, X., "A predominant role of integrin $\alpha 4$ in the spontaneous development of autoimmune diabetes in nonobese diabetic mice," <i>Proc. Natl. Acad. Sci. USA</i> , <b>1994</b> , 91, 12604-12608
	<b>BM</b>	Yednock, T.A., "Prevention of experimental autoimmune encephalomyelitis by antibodies against $\alpha 4\beta 1$ integrin," <i>Nature</i> , <b>1992</b> , 356, 63-66
	<b>BN</b>	Whitlock, B.J. et al., "Structure and synthesis of lathyrine," <i>J. Org. Chem.</i> , <b>1965</b> , 30, 115-118
	<b>BO</b>	WPI / Derwent No. XP-002076854, Japanese Patent No. <b>JP 04 193 895 A</b> (Ajinomoto, K.K.), July 13, <b>1992</b> , DW9234, 1 Page, Abstract Only
	<b>BP</b>	WPI / Derwent No. XP-002076855, Japanese Patent No. <b>JP 56 049 373 A</b> (Dainippon Pharm Co Ltd), May 2, <b>1981</b> , DW8125, 1 Page, Abstract Only
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<b>U. S. PATENT DOCUMENTS</b>						
Examiner Initial		Document No.	Date	Name	Class	Subclass
	<b>BQ</b>	4,987,132	01/22/91	Mase et al.	514	252
	<b>BR</b>	5,164,372	11/17/92	Matsuo et al.	514	19
	<b>BS</b>	5,260,277	11/09/93	McKenzie	544	18
	<b>BT</b>	5,296,486	03/22/94	Lazer et al.	514	333
<b>FOREIGN PATENT DOCUMENTS</b>						
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	<b>BU</b>	0 031 104 A1	07/01/81	EP	<input checked="" type="checkbox"/> YES	<input type="checkbox"/> NO
	<b>BV</b>	0 048 763 A1	04/07/82	EP	<input checked="" type="checkbox"/> YES	<input type="checkbox"/> NO
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	<b>CG</b>	WO 94/29285	12/22/94	PCT	X
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	<b>CJ</b>	WO 95/13811	05/26/95	PCT	X (Abstract Only)
	<b>CK</b>	WO 95/35314	12/28/95	PCT	X (Abstract Only)
	<b>CL</b>	WO 96/01644	01/25/96	PCT	X
	<b>CM</b>	WO 96/22966	08/01/96	PCT	X
	<b>CN</b>	WO 97/03094	01/30/97	PCT	X
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	<b>CQ</b>	WO 97/36859	10/09/97	PCT	X
	<b>CR</b>	WO 98/04247	02/05/98	PCT	X
	<b>CS</b>	WO 98/04913	02/05/98	PCT	X
	<b>CT</b>	WO 98/42662	10/01/98	PCT	X
	<b>CU</b>	WO 98/53814	12/03/98	PCT	X
	<b>CV</b>	WO 98/53817	12/03/98	PCT	X
	<b>CW</b>	WO 98/53818	12/03/98	PCT	X
	<b>CX</b>	WO 98/58902	12/30/98	PCT	X
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<b>FOREIGN PATENT DOCUMENTS</b>					
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**RECEIVED BY THE UNITED STATES  
PATENT AND TRADEMARK OFFICE**

**Paper:** Supplemental Information Disclosure Statement (w/first class stamp, in duplicate); USPTO Form 1449 (2 sheets); 13 references cited/all copies submitted; check in the amount of \$240.00; return postcard

**Applicant(s) :** John Robert Porter et al.

**Title:**  $\beta$ -ALANINE DERIVATIVES

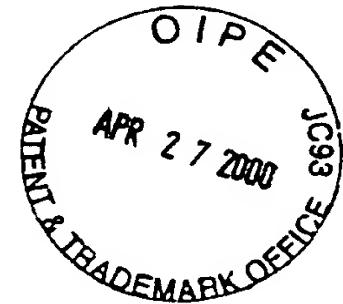
**Serial No.:** 09/450,999

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**Date Sent:** April 25, 2000

DAC:EA McLoud





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List of Patent and Publications Cited by Applicant (Use several sheets if necessary)		
U.S. Department of Commerce Patent and Trademark Office		
Docket No. <b>CELL-0086</b>		Serial No. <b>09/450,999</b>
Applicant <b>John Robert Porter, John Clifford Head,          Graham John Warrelow, and          Sarah Catherine Archibald</b>		
Filing Date <b>November 29, 1999</b>		Group <b>1624</b>
<b>OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)</b>		
	<b>AA</b>	Buckle, D.R., et al., "Non Thiazolidinedione Antihyperglycaemic Agents. 1: $\alpha$ -Heteroatom Substituted $\beta$ -Phenylpropanoic Acids," <i>Bioorg. Med. Chem. Lett.</i> , <b>1996</b> , 6(17), 2121-2126
	<b>AB</b>	Keenan, R.M. et al., "Discovery of Potent Nonpeptide Vitronectin Receptor (av $\beta_3$ ) Antagonists," <i>J. Med. Chem.</i> , <b>1997</b> , 40(15), 2289-2292
	<b>AC</b>	McDowell, R.S. et al., "From Peptide to Non-Peptide. 2. The <i>de Novo</i> Design of Potent, Non-Peptidal Inhibitors of Platelet Aggregation Based on a Benzodiazepinedione Scaffold," <i>J. Am. Chem. Soc.</i> , <b>1994</b> , 116, 5077-5083
	<b>AD</b>	Miller, W.H. et al., "Structure-Activity Relationships in 3-Oxo-1,4-Benzodiazepine-2-Acetic Acid GPIIb/IIIa Antagonists. The 2-Benzazepine Series," <i>Bioorg. Med. Chem. Lett.</i> , <b>1996</b> , 6(21), 2481-2486
	<b>AE</b>	Ukai, Y. et al., "A novel synthetic inhibitor of endopeptidase-24.15," <i>Chemical Abstracts</i> , <b>1997</b> , 127(2), 1 page
	<b>AF</b>	Venturella, V.S. et al., "Substituted 1,3-Dihydro-4H-furo[3,4- <i>d</i> ]-1,3-benzodiazepin-3-ones: Synthesis and Scope of the Method," <i>J. Heterocyclic Chem.</i> , <b>1969</b> , 6(5), 671-679
	<b>AG</b>	Wojciechowska, H. et al., "Preparation of 2,4-dinitrophenyl derivatives of tyrosine," <i>Chemical Abstracts</i> , <b>1968</b> , 68(25), Abstract No. 114926r, 1 page
<b>EXAMINER</b>		<b>DATE CONSIDERED</b>

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Sheet 2 of 2

<b>Form PTO-1449 Modified</b>  List of Patent and Publications Cited by Applicant (Use several sheets if necessary)  U.S. Department of Commerce Patent and Trademark Office		Docket No. <b>CELL-0086</b>	Serial No. <b>09/450,999</b>
		Applicant <b>John Robert Porter, John Clifford Head,          Graham John Warrelow, and          Sarah Catherine Archibald</b>	
		Filing Date <b>November 29, 1999</b>	Group <b>1624</b>

**U. S. PATENT DOCUMENTS**

<b>Examiner Initial</b>		<b>Document No.</b>	<b>Date</b>	<b>Name</b>	<b>Class</b>	<b>Subclass</b>

**FOREIGN PATENT DOCUMENTS**

<b>Examiner Initial</b>		<b>Document No.</b>	<b>Date</b>	<b>Country</b>	<b>Translation</b>	
					<b>YES</b>	<b>NO</b>
	<b>AH</b>	WO 93/00095	01/07/93	PCT	X	
	<b>AI</b>	WO 93/08174	04/29/93	PCT	X	
	<b>AJ</b>	WO 95/19356	07/20/95	PCT	X (Abstract Only)	
	<b>AK</b>	WO 96/26190	08/29/96	PCT	X	
	<b>AL</b>	JP 56 090045	07/21/81	Japan	X (Abstract Only)	
	<b>AM</b>	DE 28 37 264 A1	03/01/79	Germany	X (Abstract Only)	

**EXAMINER**

**DATE CONSIDERED**